Distinct Bone Marrow Sources of Pleiotrophin Control Hematopoietic Stem Cell Maintenance and Regeneration.

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Public Summary:

Scientific Abstract:
Bone marrow (BM) perivascular stromal cells and vascular endothelial cells (ECs) are essential for hematopoietic stem cell (HSC) maintenance, but the roles of distinct niche compartments during HSC regeneration are less understood. Here we show that Leptin receptor-expressing (LepR+) BM stromal cells and ECs dichotomously regulate HSC maintenance and regeneration via secretion of pleiotrophin (PTN). BM stromal cells are the key source of PTN during steady-state hematopoiesis because its deletion from stromal cells, but not hematopoietic cells, osteoblasts, or ECs, depletes the HSC pool. Following myelosuppressive irradiation, PTN expression is increased in bone marrow endothelial cells (BMECs), and PTN(+) ECs are more frequent in the niche. Moreover, deleting Ptn from ECs impairs HSC regeneration whereas Ptn deletion from BM stromal cells does not. These findings reveal dichotomous and complementary regulation of HSC maintenance and regeneration by BM stromal cells and ECs.